



SLC25A13 gene

solute carrier family 25 member 13

Normal Function

The *SLC25A13* gene provides instructions for making a protein called citrin. This protein is active chiefly in the liver, kidneys, and heart. Within the cells of these organs, citrin is involved in transporting molecules into and out of energy-producing structures called mitochondria. Specifically, citrin carries a protein building block (amino acid) called glutamate into mitochondria and transports the amino acid aspartate out of mitochondria as part of a process called the malate-aspartate shuttle.

An adequate supply of aspartate must be transported out of mitochondria to participate in a process called the urea cycle. The urea cycle is a sequence of chemical reactions that takes place in liver cells. These reactions process excess nitrogen that is generated as the body uses proteins. The excess nitrogen is used to make a compound called urea, which is excreted from the body in urine.

Citrin participates in several other important cellular functions as part of the malate-aspartate shuttle. This protein plays a role in producing and breaking down simple sugars and making proteins. It is also involved in the production of nucleotides, which are the building blocks of DNA and its chemical cousin, RNA.

Health Conditions Related to Genetic Changes

citrullinemia

More than 20 mutations in the *SLC25A13* gene have been identified in people with adult-onset type II citrullinemia. Almost all of the identified mutations lead to the production of an unstable citrin protein that is quickly broken down or an abnormally short, nonfunctional version of the protein.

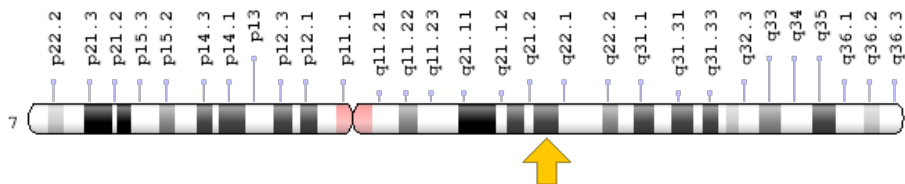
A lack of functional citrin blocks the malate-aspartate shuttle, including the transport of aspartate out of mitochondria. This loss of citrin inhibits the normal production of proteins and nucleotides. It also reduces the amount of aspartate available to take part in the urea cycle. As a result, the liver cannot effectively process excess nitrogen into urea. A disruption in the urea cycle allows nitrogen (in the form of ammonia) and other byproducts of the urea cycle (such as citrulline) to build up in the bloodstream. Ammonia is toxic, especially to the nervous system, which helps explain the development of abnormal behaviors and other neurologic problems in people with adult-onset type II citrullinemia.

Mutations in the *SLC25A13* gene also have been found in infants with a liver disorder called neonatal intrahepatic cholestasis caused by citrin deficiency (NICCD). This liver disorder is also known as neonatal-onset type II citrullinemia. NICCD blocks the flow of bile (a digestive fluid produced by the liver) and prevents the body from processing certain nutrients properly. Ammonia does not build up in the bloodstream of infants with NICCD, and the signs and symptoms typically resolve within a year. Many infants with NICCD have the same mutations in the *SLC25A13* gene as people with adult-onset type II citrullinemia. Years or even decades later, some people who had NICCD as infants develop the characteristic features of adult-onset type II citrullinemia.

Chromosomal Location

Cytogenetic Location: 7q21.3, which is the long (q) arm of chromosome 7 at position 21.3

Molecular Location: base pairs 96,120,220 to 96,322,147 on chromosome 7 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- ARALAR2
- calcium-binding mitochondrial carrier protein Aralar2
- CITRIN
- CMC2_HUMAN
- CTLN2
- mitochondrial aspartate glutamate carrier 2
- solute carrier family 25 (aspartate/glutamate carrier), member 13

Additional Information & Resources

Educational Resources

- Chapter 23.4: Ammonium Ion Is Converted Into Urea in Most Terrestrial Vertebrates (Biochemistry, fifth edition, 2002)
<https://www.ncbi.nlm.nih.gov/books/NBK22450/>

GeneReviews

- Citrin Deficiency
<https://www.ncbi.nlm.nih.gov/books/NBK1181>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28SLC25A13%5BTIAB%5D%29+OR+%28solute+carrier+family+25,+member+13%5BTIAB%5D%29%29+OR+%28%28ARALAR2%5BTIAB%5D%29+OR+%28CITRIN%5BTIAB%5D%29+OR+%28CTLN2%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+2160+days%22%5Bdp%5D>

OMIM

- CITRULLINEMIA, TYPE II, NEONATAL-ONSET
<http://omim.org/entry/605814>
- SOLUTE CARRIER FAMILY 25 (CITRIN), MEMBER 13
<http://omim.org/entry/603859>

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
http://atlasgeneticsoncology.org/Genes/GC_SLC25A13.html
- ClinVar
<https://www.ncbi.nlm.nih.gov/clinvar?term=SLC25A13%5Bgene%5D>
- HGNC Gene Family: EF-hand domain containing
<http://www.genenames.org/cgi-bin/genefamilies/set/863>
- HGNC Gene Family: Solute carriers
<http://www.genenames.org/cgi-bin/genefamilies/set/752>
- HGNC Gene Symbol Report
http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=10983

- NCBI Gene
<https://www.ncbi.nlm.nih.gov/gene/10165>
- UniProt
<http://www.uniprot.org/uniprot/Q9UJS0>

Sources for This Summary

- Kobayashi K, Bang Lu Y, Xian Li M, Nishi I, Hsiao KJ, Choeh K, Yang Y, Hwu WL, Reichardt JK, Palmieri F, Okano Y, Saheki T. Screening of nine SLC25A13 mutations: their frequency in patients with citrin deficiency and high carrier rates in Asian populations. *Mol Genet Metab*. 2003 Nov;80(3):356-9.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/14680984>
- Lu YB, Kobayashi K, Ushikai M, Tabata A, Iijima M, Li MX, Lei L, Kawabe K, Taura S, Yang Y, Liu TT, Chiang SH, Hsiao KJ, Lau YL, Tsui LC, Lee DH, Saheki T. Frequency and distribution in East Asia of 12 mutations identified in the SLC25A13 gene of Japanese patients with citrin deficiency. *J Hum Genet*. 2005;50(7):338-46. Epub 2005 Jul 30.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/16059747>
- Ohura T, Kobayashi K, Tazawa Y, Nishi I, Abukawa D, Sakamoto O, Iinuma K, Saheki T. Neonatal presentation of adult-onset type II citrullinemia. *Hum Genet*. 2001 Feb;108(2):87-90.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/11281457>
- Saheki T, Kobayashi K, Iijima M, Horiuchi M, Begum L, Jalil MA, Li MX, Lu YB, Ushikai M, Tabata A, Moriyama M, Hsiao KJ, Yang Y. Adult-onset type II citrullinemia and idiopathic neonatal hepatitis caused by citrin deficiency: involvement of the aspartate glutamate carrier for urea synthesis and maintenance of the urea cycle. *Mol Genet Metab*. 2004 Apr;81 Suppl 1:S20-6. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/15050970>
- Saheki T, Kobayashi K, Iijima M, Moriyama M, Yazaki M, Takei Y, Ikeda S. Metabolic derangements in deficiency of citrin, a liver-type mitochondrial aspartate-glutamate carrier. *Hepatol Res*. 2005 Oct;33(2):181-4. Epub 2005 Sep 30.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/16199199>
- Saheki T, Kobayashi K, Iijima M, Nishi I, Yasuda T, Yamaguchi N, Gao HZ, Jalil MA, Begum L, Li MX. Pathogenesis and pathophysiology of citrin (a mitochondrial aspartate glutamate carrier) deficiency. *Metab Brain Dis*. 2002 Dec;17(4):335-46. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/12602510>
- Saheki T, Kobayashi K. Mitochondrial aspartate glutamate carrier (citrin) deficiency as the cause of adult-onset type II citrullinemia (CTLN2) and idiopathic neonatal hepatitis (NICCD). *J Hum Genet*. 2002;47(7):333-41. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/12111366>

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